REMARKS

Claims 2, 3, 6, 7, 9, 10, 12, 13, 15, 16, and 18-26 are active in this application.

The rejection of Claims 2, 3, 6, 7, 9, 10, 12, 13, 15, 16, and 18-23 under 35 U.S.C. §101 is traversed.

Applicants again bring the Examiner's attention to *Diamond v. Chakrabarty* which states: "in the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter." However, this is *certainly* not the case in the present application. Applicants wish to draw the Examiner's attention to the claims reproduced above, which specifically state: "***isolated*** coryneform bacterium." Again, Applicants know of no other means of isolation, but by the hands of man. As such, the present claims are, without question, statutory subject matter.

Despite failing to provide any possible means by which the artisan may isolate coryneform bacterium, but by the hands of man, the Examiner has maintained his position that the recitation of the term "isolated" fails to distinguish the presently claimed bacterium from that which can be found in nature. Applicants wish to bring the Examiner's attention to US 6,261,824 and US 6,344,344 (**copies enclosed herewith**) in which the Office has already taken the position that the adjective "isolated" used to qualify "bacterium" is compliant with 35 U.S.C. §101. Applicants wonder whether it is the Examiner's intention to throw Office precedent out the window and to rewrite this preexisting precedent.

In view of the foregoing, Applicants request withdrawal of this ground of rejection.

The rejections of Claims 2, 3, 6, 7, 9, 10, 12, 13, 15, 16, and 18-23 under 35 U.S.C. §112, first paragraph ("written description" and "enablement"), are respectfully traversed.

The independent claim as amended herewith is Claim 2, which recites:

An isolated coryneform bacterium wherein an argR gene on a chromosome of the bacterium is disrupted, and the argR gene has the nucleotide sequence shown in SEQ ID NO:17 or is obtained from chromosomal DNA of the bacterium by PCR under a condition with oligonucleotide primers having a nucleotide sequence shown in SEQ ID NO:15 and SEQ ID NO:16, wherein the condition is a condition in which annealing is performed at 58°C.

There is no question that SEQ ID NO:17 is described in the specification, see, for example, the Sequence Listing. Moreover, Applicants note that objected to "degree of homology that it can homologously recombine with the nucleotide sequence shown in SEQ ID NO:17" has been amended recite "obtained from chromosomal DNA of the bacterium by PCR with oligonucleotide primers having a nucleotide sequence shown in SEQ ID NO:15 and SEQ ID NO:16." In this regard, Applicants note that the determination of PCR conditions would be readily appreciated by one of skill in the art with the present application in hand. Specifically, Applicants note that Example 3 (pages 25-30) clearly direct the artisan on how to make and use the present invention. As such, Applicants submit that one possessing much less than routine skill in the art can practice the present invention.

Applicants note that this ground of rejection is based on the Examiner's perception that the PCR product of SEQ ID NO: 15 and SEQ ID NO: 16 would embrace a large number of sequences of diverse sequence and structure. Applicants disagree with this assertion by the Examiner. In particular, Applicants note that each of SEQ ID NOs: 15 and 16 are 25 nucleotides long and, as such, their statistical occurrence in the genome would be on the order

of 1 per 1 x 10^{15} bp[1]. In contrast bacterial genomes, such as coryneform bacteria only have about 1 x 10^6 bp. Accordingly, even under low stringency conditions, which permit mismatches in the primer hybridization step, PCR would still be expected to produce the target gene. This is especially true when the high sequence homology of argR genes among coryneform bacteria is taken into account (page 14, lines 8-13). In fact, the high homology of argR gene would further simplify the screening and analysis to verify that the gene obtained by PCR is actually the argR gene.

Moreover, Applicants remind the Examiner that MPEP §2164.05(a) states:

> The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public... The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date.

In this instance, PCR conditions including the temperature and buffer conditions required to ensure adequate stringency such as to reduce faulty priming would be readily appreciated to the artisan. As the Examiner surely can not contest, PCR methods, conditions, and protocols are "old hat" for the skilled artisan and, thus, it is not the burden of the Applicants to detail each and every permutation of the technology that would result in the genes within the scope of the claimed invention. In fact, the Office encourages that Applicants not burden them with such well-known methods. Despite this Office mandate, Applicants note that Example 2 on page 23, line 21 to page 25, line 19 provides exemplary PCR conditions for the primer pair of SEQ ID NOs: 15 and 16.

Moreover, one skilled in the art can readily determine conditions which are sufficient to amplify at least an internal protion of the argR gene as presently claimed. For example, the skilled artisan may perform PCR experiments while changing the annealing temperature, and

[1] $N = 4^{25} = 1.12 \times 10^{15}$

then examining whether or not there is an argR gene in the PCR product. Applicants further note that several permutations of this technique and/or alternatives to the same are readily available through one of many treatises on PCR methodologies.

In view of the foregoing, Applicants submit that with the specification in hand, coupled with the knowledge generally available in the art, the skilled artisan would readily appreciate how to make and use the invention as claimed. As such, Applicants note that the presently claimed invention meets both prongs of the 35 U.S.C. §112, first paragraph, analysis (written description and enablement). Therefore, withdrawal of the rejections under 35 U.S.C. §112, first paragraph, is requested.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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